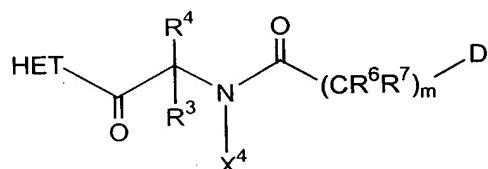


Claims

5 1. A compound of the formula



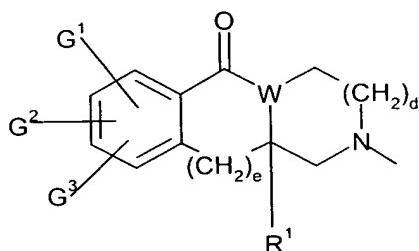
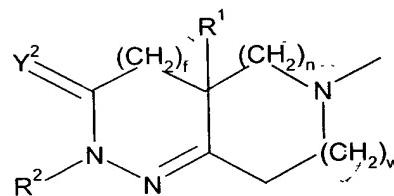
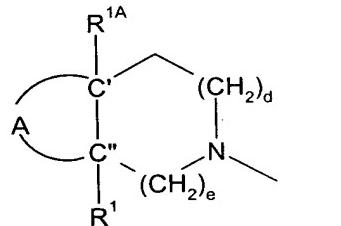
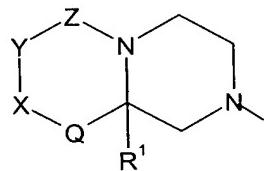
or a stereoisomeric mixture thereof, diastereomerically enriched, diastereomerically pure, enantiomerically enriched or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture or isomer thereof, or a pharmaceutically acceptable salt

10 of the compound, mixture, isomer or prodrug,

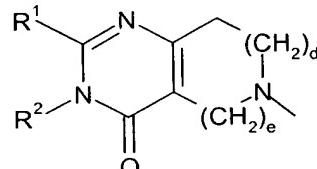
wherein:

m is 0, 1 or 2;

HET is a heterocyclic moiety selected from the group consisting of



and



15 d is 0, 1 or 2;

e is 1 or 2;

f is 0 or 1;

n and w are 0, 1 or 2, provided that n and w cannot both be 0 at the same time;

5 Y² is oxygen or sulfur;

A is a radical, where the left hand side of the radical as shown below

is connected to C" and the right hand side of the radical as shown below is connected to C', selected from the group consisting of -NR²-C(O)-NR²-, -NR²-S(O)₂-NR²-, -O-C(O)-NR²-, -NR²-C(O)-O-, -C(O)-NR²-C(O)-, -C(O)-NR²-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-NR²-C(O)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -S(O)₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-O-C(O)-, -C(R⁹R¹⁰)-O-C(R⁹R¹⁰)-, -NR²-C(O)-C(R⁹R¹⁰)-, -O-C(O)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(O)-NR²-C(O)-NR²-C(O)-O-, -C(R⁹R¹⁰)-C(O)-O-, -C(O)-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(O)-O-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -S(O)₂-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-NR²-C(O)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-O-C(O)-, -NR²-C(O)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -NR²-S(O)₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -O-C(O)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(O)-NR²-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(O)-, -C(R⁹R¹⁰)-NR²-C(O)-O-, -C(R⁹R¹⁰)-O-C(R⁹R¹⁰)-, -NR²-C(O)-O-C(R⁹R¹⁰)-, -NR²-C(O)-NR²-C(R⁹R¹⁰)-, -NR²-S(O)₂-NR²-C(R⁹R¹⁰)-, -O-C(O)-NR²-C(R⁹R¹⁰)-, -C(O)-N=C(R¹¹)-NR²-, -C(O)-NR²-C(R¹¹)=N-, -C(R⁹R¹⁰)-NR¹²-C(R⁹R¹⁰)-, -NR¹²-C(R⁹R¹⁰)-,

10 -NR¹²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(O)-O-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -NR²-C(R¹¹)=N-C(O)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-N(R¹²)-, -C(R⁹R¹⁰)-NR¹²-, -N=C(R¹¹)-NR²-C(O)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-NR²-S(O)₂-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-S(O)₂-NR²-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(O)-O-, -C(R⁹R¹⁰)-S(O)₂-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-S(O)₂-, -O-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-O-, -C(R⁹R¹⁰)-C(O)-C(R⁹R¹⁰)-, -C(O)-C(R⁹R¹⁰)-C(R⁹R¹⁰)- and -C(R⁹R¹⁰)-NR²-S(O)₂-NR²-;

25 Q is a covalent bond or CH₂;

W is CH or N;

X is CR⁹R¹⁰, C=CH₂ or C=O;

Y is CR⁹R¹⁰, O or NR²;

30 Z is C=O, C=S or S(O)₂;

G¹ is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, -CONH₂, -(C₁-C₄)alkyl optionally independently substituted with one or more phenyl, one or more halogens or one or more hydroxy groups, -(C₁-C₄)alkoxy optionally independently substituted with one or more phenyl, one or more halogens or one or

more hydroxy groups, -(C₁-C₄)alkylthio, phenoxy, -COO(C₁-C₄)alkyl, N,N-di-(C₁-C₄)alkylamino, -(C₂-C₆)alkenyl optionally independently substituted with one or more phenyl, one or more halogens or one or more hydroxy groups, -(C₂-C₆)alkynyl optionally independently substituted with one or more phenyl, one or more halogens or one or more hydroxy groups, -(C₃-C₆)cycloalkyl optionally independently substituted with one or more (C₁-C₄)alkyl groups, one or more halogens or one or more hydroxy groups, -(C₁-C₄)alkylamino carbonyl or di-(C₁-C₄)alkylamino carbonyl;

G² and G³ are each independently selected from the group consisting of hydrogen, halo, hydroxy, -(C₁-C₄)alkyl optionally independently substituted with one to three halogens and -(C₁-C₄)alkoxy optionally independently substituted with one to three halogens;

R¹ is hydrogen, -(CH₂)_qN(X⁶)C(O)X⁶, -(CH₂)_qN(X⁶)C(O)(CH₂)_tA¹, -(CH₂)_qN(X⁶)S(O)₂(CH₂)_tA¹, -(CH₂)_qN(X⁶)S(O)₂X⁶, -(CH₂)_qN(X⁶)C(O)N(X⁶)(CH₂)_tA¹, -(CH₂)_qN(X⁶)C(O)N(X⁶)(X⁶), -(CH₂)_qC(O)N(X⁶)(X⁶), -(CH₂)_qC(O)N(X⁶)(CH₂)_tA¹, -(CH₂)_qC(O)OX⁶, -(CH₂)_qC(O)O(CH₂)_tA¹, -(CH₂)_qOX⁶, -(CH₂)_qOC(O)X⁶, -(CH₂)_qOC(O)(CH₂)_tA¹, -(CH₂)_qOC(O)N(X⁶)(CH₂)_tA¹, -(CH₂)_qOC(O)N(X⁶)(X⁶), -(CH₂)_qC(O)X⁶, -(CH₂)_qC(O)(CH₂)_tA¹, -(CH₂)_qN(X⁶)C(O)OX⁶, -(CH₂)_qN(X⁶)S(O)₂N(X⁶)(X⁶), -(CH₂)_qS(O)_mX⁶, -(CH₂)_qS(O)_m(CH₂)_tA¹, -(C₁-C₁₀)alkyl, -(CH₂)_tA¹, -(CH₂)_q-(C₃-C₇)cycloalkyl, -(CH₂)_q-Y¹-(C₁-C₆)alkyl, -(CH₂)_q-Y¹-(CH₂)_t-(C₃-C₇)cycloalkyl;

where the alkyl and cycloalkyl groups in the definition of R¹ are optionally substituted with (C₁-C₄)alkyl, hydroxy, (C₁-C₄)alkoxy, carboxyl, -CONH₂, -S(O)_m(C₁-C₆)alkyl, -CO₂(C₁-C₄)alkyl ester, 1H-tetrazol-5-yl or 1, 2 or 3 fluoro groups;

Y¹ is O, S(O)_m, -C(O)NX⁶-, -CH=CH-, -C≡C-, -N(X⁶)C(O)-, -C(O)NX⁶-, -C(O)O-, -OC(O)N(X⁶)- or -OC(O)-;

q is 0, 1, 2, 3 or 4;

t is 0, 1, 2 or 3;

said (CH₂)_q group and (CH₂)_t group in the definition of R¹ are optionally independently substituted with hydroxy, (C₁-C₄)alkoxy, carboxyl, -CONH₂, -S(O)_m(C₁-C₆)alkyl, -CO₂(C₁-C₄)alkyl ester, 1H-tetrazol-5-yl, 1, 2 or 3 fluoro groups or 1 or 2 (C₁-C₄)alkyl groups;

R^{1A} is selected from the group consisting of hydrogen, F, Cl, Br, I, (C₁-C₆)alkyl, phenyl(C₁-C₃)alkyl, pyridyl(C₁-C₃)alkyl, thiazolyl(C₁-C₃)alkyl and thieryl(C₁-C₃)alkyl, provided that R^{1A} is not F, Cl, Br or I when a heteroatom is vicinal to C";

R², for each occurrence, is independently hydrogen, (C₁-C₈)alkyl, -(C₀-C₃)alkyl-(C₃-C₈)cycloalkyl, -(C₁-C₄)alkyl-A¹ or A¹;

where the alkyl groups and the cycloalkyl groups in the definition of R² are optionally substituted with hydroxy, -C(O)OX⁶, -C(O)N(X⁶)(X⁶), -N(X⁶)(X⁶),

5 -S(O)_m(C₁-C₆)alkyl, -C(O)A¹, -C(O)(X⁶), CF₃, CN or 1, 2 or 3 independently selected halogens;

R³ and R⁴ are each independently selected from the group consisting of hydrogen, (C₁-C₈)alkyl, -CH(R⁸)-aryl, -CH(R⁸)-heteroaryl, -(C₀-C₃)alkyl(C₃-C₈)cycloalkyl, wherein the aryl or heteroaryl groups are optionally substituted by one

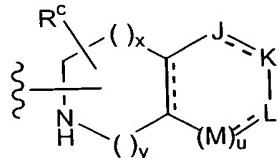
10 or two R^b groups;

R^b, for each occurrence independently, is R^c, halo, -OR^c, -NHSO₂R^c, -N(R^c)₂, -CN, -NO₂, -SO₂N(R^c)₂, -SO₂R^c, -CF₃, -OCF₃; -OCF₂H or two R^b groups attached to adjacent carbon atoms taken together to form methylenedioxy;

15 R^c, for each occurrence independently, is hydrogen, -(C₁-C₈)alkyl, -(C₀-C₃)alkylaryl, -(C₀-C₃)alkylheteroaryl, (C₃-C₆)cycloalkyl; or 2 R^b taken together with the nitrogen atom to which they are attached to form a 5- or 6- membered ring optionally containing an additional heteroatom selected from O, S or NR³;

20 R⁶ and R⁷ are each independently selected from hydrogen, (C₁-C₆)alkyl, -(C₀-C₃)alkylaryl, -(C₀-C₃)alkylheteroaryl, -(C₀-C₃)alkyl(C₃-C₈)cycloalkyl; or R⁶ and R⁷ together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally containing an additional heteroatom selected from O, S, NR³;

25 D is -(C₀-C₆)alkyl-amino-C(=NR⁷)-NR¹⁵R¹⁶, -(C₀-C₆)alkylaminopyridyl, -(C₀-C₆)alkylaminoimidazolyl, -(C₀-C₆)alkylaminothiazolyl, -(C₀-C₆)alkylaminopyrimidinyl, (C₀-C₆)alkylaminopiperazinyl-R¹⁵, -(C₀-C₆)alkylmorpholinyl, wherein R¹⁵ and R¹⁶ are independently hydrogen, -(C₁-C₆)alkyl, -(C₀-C₃)alkylaryl, -(C₀-C₃)alkylheteroaryl, -(C₀-C₃)alkyl(C₃-C₈)cycloalkyl, wherein the alkyl and aryl groups are optionally substituted with one or two R^b groups; or D is a group of the formula



- u is 0 or 1;
- x and y are each independently 0, 1 or 2;
- J, K, L and M are each independently selected from C(R^b)_r, N, S or O wherein R^b and R^c are as defined above and r is 1 or 2;
- 5 X⁴ is hydrogen or (C₁-C₆)alkyl or X⁴ is taken together with R⁴ and the nitrogen atom to which X⁴ is attached and the carbon atom to which R⁴ is attached and form a five to seven membered ring;
- 10 R⁸ is hydrogen, -(C₁-C₈)alkyl, -(C₀-C₃)alkylaryl, -(C₀-C₃)alkylheteroaryl, -(C₃-C₆)cycloalkyl; or 2 R^b taken together with the nitrogen atom to which they are attached to form a 5- or 6- membered ring optionally containing an additional heteroaryl selected from O, S or NR³;
- 15 R⁹ and R¹⁰, for each occurrence, are each independently selected from the group consisting of hydrogen, fluoro, hydroxy and (C₁-C₅)alkyl optionally independently substituted with 1-5 halogens;
- 20 R¹¹ is selected from the group consisting of (C₁-C₅)alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of (C₁-C₅)alkyl, halo and (C₁-C₅)alkoxy;
- 25 R¹² is selected from the group consisting of (C₁-C₅)alkylsulfonyl, (C₁-C₅)alkanoyl and (C₁-C₅)alkyl where the alkyl portion is optionally independently substituted by 1-5 halogens;
- 30 A¹ for each occurrence is independently selected from the group consisting of (C₅-C₇)cycloalkenyl, phenyl, a partially saturated, fully saturated or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen and a bicyclic ring system consisting of a partially saturated, fully unsaturated or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen, fused to a partially saturated, fully saturated or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur and oxygen;
- 35 A¹ for each occurrence is independently optionally substituted, on one or optionally both rings if A¹ is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, -OCF₃, -OCF₂H, -CF₃, -CH₃, -OCH₃, -OX⁶,

- DECODED DOCUMENT
- C(O)N(X⁶)(X⁶), -C(O)OX⁶, oxo, (C₁-C₆)alkyl, nitro, cyano, benzyl,
-S(O)_m(C₁-C₆)alkyl, 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy,
halophenyl, methylenedioxy, -N(X⁶)(X⁶), -N(X⁶)C(O)(X⁶), -S(O)₂N(X⁶)(X⁶),
-N(X⁶)S(O)₂-phenyl, -N(X⁶)S(O)₂X⁶, -CONX¹¹X¹², -S(O)₂NX¹¹X¹²,
5 -NX⁶S(O)₂X¹², -NX⁶CONX¹¹X¹², -NX⁶S(O)₂NX¹¹X¹², -NX⁶C(O)X¹², imidazolyl,
thiazolyl and tetrazolyl, provided that if A¹ is optionally substituted with
methylenedioxy then it can only be substituted with one methylenedioxy;
where X¹¹, for each occurrence, is independently hydrogen or
optionally substituted (C₁-C₆)alkyl;
- 10 the optionally substituted (C₁-C₆)alkyl defined for X¹¹ is
optionally independently substituted with phenyl, phenoxy, (C₁-
C₆)alkoxycarbonyl, -S(O)_m(C₁-C₆)alkyl, 1 to 5 halogens, 1 to 3
hydroxy groups, 1 to 3 (C₁-C₁₀)alkanoyloxy groups or 1 to 3
(C₁-C₆)alkoxy groups;
- 15 X¹², for each occurrence, is independently hydrogen, (C₁-C₆)alkyl,
phenyl, thiazolyl, imidazolyl, furyl or thienyl, provided that when X¹² is
not hydrogen, the X¹² group is optionally substituted with one to three
substituents independently selected from the group consisting of Cl, F,
CH₃, OCH₃, OCF₃ and CF₃;
- 20 or X¹¹ and X¹² are taken together to form -(CH₂)_gL¹-(CH₂)_g-;
L¹ is C(X²)(X²), O, S(O)_m or N(X²);
g for each occurrence is independently 1, 2 or 3;
X² for each occurrence is independently hydrogen, optionally substituted (C₁-
C₆)alkyl or optionally substituted (C₃-C₇)cycloalkyl, where the optionally substituted
25 (C₁-C₆)alkyl and optionally substituted (C₃-C₇)cycloalkyl in the definition of X² are
optionally independently substituted with -S(O)_m(C₁-C₆)alkyl, -C(O)OX³, 1 to 5
halogens or 1-3 OX³ groups;
X³ for each occurrence is independently hydrogen or (C₁-C₆)alkyl;
X⁶ for each occurrence is independently hydrogen, optionally substituted (C₁-
30 C₆)alkyl, (C₂-C₆)halogenated alkyl, optionally substituted (C₃-C₇)cycloalkyl, (C₃-C₇)-
halogenated cycloalkyl, where optionally substituted (C₁-C₆)alkyl and optionally
substituted (C₃-C₇)cycloalkyl in the definition of X⁶ is optionally independently mono-
or di-substituted with (C₁-C₄)alkyl, hydroxy, (C₁-C₄)alkoxy, carboxyl, CONH₂,
-S(O)_m(C₁-C₆)alkyl, carboxylate (C₁-C₄)alkyl ester or 1H-tetrazol-5-yl; or

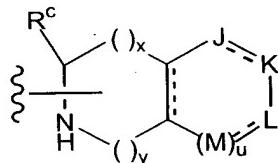
when there are two X^6 groups on one atom and both X^6 are independently (C_1 - C_6)alkyl, the two (C_1 - C_6)alkyl groups may be optionally joined and, together with the atom to which the two X^6 groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur or NX^7 as a ring member;

- 5 X^7 is, for each occurrence independently, hydrogen or (C_1 - C_6)alkyl optionally substituted with hydroxy;

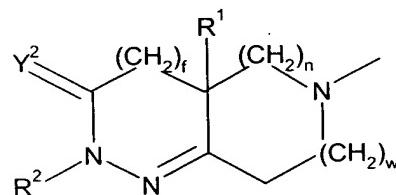
 m for each occurrence is independently 0, 1 or 2;

 with the proviso that: X^6 and X^{12} cannot be hydrogen when attached to C(O) or S(O)₂ in the form C(O) X^6 , C(O) X^{12} , S(O)₂ X^6 or S(O)₂ X^{12} .

- 10 2. A compound according to claim 1, wherein D is



3. A compound according to claim 2, wherein x is 1, y is 1 and u is 1.
4. A compound according to claim 3, wherein J, K, L and M are each
15 NR^b or C(R^b)_r where r = 1 or 2, R⁴ is -CH₂-aryl in which aryl is optionally substituted by R^b.
5. A compound according to claim 4, wherein HET is



- 20 6. A compound according to claim 5, wherein Y² is oxygen, f is 0, n is 1 or 2; and w is 0 or 1.

7. A compound according to claim 6, wherein R² is (C_1 - C_6)alkyl optionally substituted by halo, R³ is hydrogen, n is 1, w is 1, and R¹ is aryl(C_1 - C_6)alkyl, (C_1 - C_6)alkyl or heteroaryl(C_1 - C_6)alkyl wherein aryl and heteroaryl are optionally substituted with one or two groups from the following list: halo, -OR^c, -NHSO₂R^c, -N(R^c)₂, -CN, -NO₂, -SO₂N(R^c)₂, -SO₂R^c, -CF₃, -OCF₃; -OCF₂H.

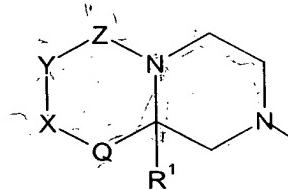
8. A compound according to claim 7, wherein J, K, L and M are each N or CR^b and the dashed lines represent double bonds, R¹ is benzyl optionally substituted by halo, -R^c, -OR^c, -CF₃, -OCF₃, -OCF₂H, R^c, hydrogen, -(C₁-C₆)alkyl,
5 -(C₀-C₃)alkylaryl, -(C₀-C₃)alkylheteroaryl or -(C₃-C₆)cycloalkyl.
9. A compound according to claim 1, wherein said compound is selected from the group consisting of:
- 1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid [2-((R)3a-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-(R)1-(4-chlorobenzyl)-2-oxo-ethyl]-amide;
- 10 1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid [2-((R3a-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-(R)1-(4-chlorobenzyl)-2-oxo-ethyl]-amide;
- 1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid [2-[3a-benzyl-3-oxo-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-(R)1-(4-chloro-benzyl)-2-oxo-ethyl]-amide;
- 15 1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid {((R)1-(4-chloro-benzyl)-2-[2-ethyl-(S)3a-(4-fluoro-benzyl)-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-2-oxo-ethyl}-amide;
- 1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {((R)1-(4-chloro-benzyl)-2-[2-ethyl-(S)3a-(4-fluoro-benzyl)-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-2-oxo-ethyl}-amide;
- 20 1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {((R)1-(4-chloro-benzyl)-2-[(S)3a-(4-chloro-benzyl)-2-ethyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-2-oxo-ethyl}-amide;
- 1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {((R)1-(4-chloro-benzyl)-2-[(S)3a-(4-chloro-benzyl)-2-ethyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-2-oxo-ethyl}-amide;
- 25 1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid {((R)1-(4-chloro-benzyl)-2-[(S)3a-(4-chloro-benzyl)-2-ethyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-2-oxo-ethyl}-amide;
- 1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid [2-((S)3a-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-(R)1-(4-chlorobenzyl)-2-oxo-ethyl]-amide;
- 30 1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid {((R)1-(4-chloro-benzyl)-2-[(R)3a-(3-fluoro-benzyl)-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]-2-oxo-ethyl}-amide;

1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid [2-[3a-benzyl-3-oxo-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl]- (R)1-(4-chloro-benzyl)-2-oxo-ethyl]-amide; and

5 1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid [(R)1-(4-chloro-benzyl)-2-oxo-2-(3-oxo-3a-pyridin-2-ylmethyl-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3-c]pyridin-5-yl)-ethyl]-amide.

10 10. A compound according to claim 7, wherein J, K, L and M are each NR^b or C(R^b)₂ and the dashed lines represent single bonds, wherein R^b is hydrogen, halo, R^c, -OR^c, -CF₃, -OCF₃, -OCF₂H, R^c is hydrogen, (C₁-C₈)alkyl, (C₀-C₃)alkylaryl, (C₀-C₃)alkylheteroaryl or -(C₃-C₆)cycloalkyl.

11. A compound according to claim 4, wherein HET is



12. A compound according to claim 11, wherein Q is a covalent bond; X and Z are each C=O; and Y is NR².

15 13. A compound according to claim 12, wherein R² is (C₁-C₆)alkyl optionally substituted by halo, and R¹ is aryl(C₁-C₆)alkyl, (C₁-C₆)alkyl or heteroaryl (C₁-C₆)alkyl wherein aryl and heteroaryl are optionally substituted with one or two groups from the following list: halo, OR^c, -NHSO₂R^c, N(R^c)₂, CN, NO₂, SO₂N(R^c)₂, -SO₂R^c, -CF₃, -OCF₃, -OCF₂H.

20 14. A compound according to claim 13, wherein J, K, L and M are each N or CR^b and the dashed lines represent double bonds, R¹ is benzyl optionally substituted by halo, -R^c, -OR^c, -OCF₃, -OCF₂H, and R^c is hydrogen, -(C₁-C₈)alkyl, -(C₀-C₃)alkylaryl, -(C₀-C₃)alkylheteroaryl or -(C₃-C₆)cycloalkyl.

25 15. A compound according to claim 1, wherein said compound is selected from the group consisting of:

1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[1,3-dioxo-(S)8a-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide;

1,2,3,4-Tetrahydro-isoquinoline-(R)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[(R)8a-(4-fluoro-benzyl)-2-methyl-1,3-dioxo-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide;

5 1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[1,3-dioxo-(S)8a-pyridin-3-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide;

10 1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[8a-(4-fluoro-benzyl)-3-oxo-tetrahydro-oxazolo[3,4-a]pyrazin-7-yl]-2-oxo-ethyl}-amide;

15 1,2,3,4-Tetrahydro-isoquinoline-(S)3-carboxylic acid {(R)1-(4-chloro-benzyl)-2-[8a-(4-fluoro-benzyl)-2-methyl-1,3-dioxo-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-amide; and

20 16. A compound according to claim 13, wherein J, K, L and M are each NR^b or C(R^b)₂ and the dashed lines represent single bonds, R^b is hydrogen, halo, R^c, OR^c, -CF₃, -OCF₃, -OCF₂H, R^c is hydrogen, -C₁-C₈)akyl, -(C₀-C₃)alkylaryl, -(C₀-C₃)alkylheteroaryl or -(C₃-C₆)cycloalkyl.

25 17. A method for the treatment or prevention of disorders, diseases or conditions responsive to the activation of melanocortin receptor which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

30 18. A method for the treatment or prevention of obesity which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

35 19. A method for the treatment or prevention of diabetes mellitus which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

40 20. A method for the treatment or prevention of male or female sexual dysfunction which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

45 21. A method for the treatment or prevention of erectile dysfunction which

comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

22. A method for modulating appetite and metabolic rates of mammals which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

23. A method for treating or preventing disorders that cause reduction in appetite, feeding behavior and/or body weight in a mammal which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

10 24. A method for acutely stimulating the appetite of companion animals for the treatment of hepatic lipidosis, cachexia and other pathologies resulting in/from inappropriate food intake and weight loss, which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

15 25. A method for acutely stimulating the appetite of livestock for the treatment of ketosis, postpartum anestrus, and other metabolic and reproductive pathologies resulting in/from inappropriate food intake and weight loss which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

20 26. A method that will enhance growth and survivability of neonates in livestock which comprises administering to a mammal in need of such treatment or prevention an effective amount of a compound of Claim 1.

27. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

25 28. A pharmaceutical composition of claim 27 further comprising a second active ingredient selected from an insulin sensitizer, insulin mimetic, sulfonylurea, α -glucosidase inhibitor, HMG-CoA reductase inhibitor, sequestrant cholesterol lowering agent, β 3 adrenergic receptor agonists, neuropeptide Y antagonist, phosphodiester V inhibitor, and α -2 adrenergic receptor antagonist.

DRAFT - 06/26/01